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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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EXAMINER
[illegible]

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 09/11/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

1. Formal Matters:

This application was filed under 35 U.S.C. 371, and since all of the claims were examined in the PCT parent application, a restriction will not be imposed herein even though a lack of unity claim can be made. Accordingly, this office action is directed to the merits of all of claims 1-35.

Since this is a 35 U.S.C. 371 application, and applicants have copies of the prior art being relied upon as a result of filing the form 905, no further copies of the art being relied upon with set issued with this office action.

2. Sequence compliance:

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures.

Applicant is given ONE MONTH, or THIRTY DAYS, whichever is longer, from the mailing date of this letter within which to comply with the sequence rules, 37 CFR 1.821 - 1.825. Failure to comply with these requirements will result in ABANDONMENT of the application under 37 CFR 1.821(g). Extensions of time may be obtained by filing a petition accompanied by the extension fee under the provisions of 37 CFR 1.136(a). In no case may an applicant extend the period for reply beyond the SIX MONTH statutory period. Direct the reply to the undersigned. Applicant is requested to return a copy of the attached Notice to Comply with the reply.

It is not clear from the specification that a disk has been filed, nor if there was full compliance in the parent application for the sequence. Additional, there is no request to use the sequence, if correct, from the parent PCT. Therefore, applicants must comply with the sequence rules for the disclosed sequence with all of the necessary averments.

3. 35 USC 112 objections and rejections:

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 4-5, 8-17, 27-34 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 4 and 11 are indefinite and confusing in the terms "peptide conformational analog" because it is not clear what the metes and bounds of this limitation is.

Regarding claims 5 and 12, the phrase "OB-related peptide" is similar to the term "or the like" and thus renders the claim(s) indefinite in the same manner because the claim(s) include(s) elements not actually disclosed (those encompassed by "or the like"), thereby rendering the scope of the claim(s) unascertainable. See MPEP § 2173.05(d). Also, the claims fail to set forth what the relationship is and how it is related? Is it a functional or structural relationship? Correction is requested.

Claims 8-17, 28-31 and 34 are directed to composition, wherein different statements of intended use are recited in these claims. The claims are indefinite for failing to recite a sufficient number of elements to support the preamble recitation for a composition. To satisfy this limitation, the claims must recite at least two elements. Thus, amending the claims to recite a carrier or other auxiliary agent or components would obviate this rejection.

Claims 32-33 are indefinite and incomplete for failing to recite sufficient elements and both physical and structural features to satisfy the preamble limitation for a kit.

Claim 27 is indefinite in the recitation of "condition characterized by OB resistance" because the nature of the condition is not specified and it is not clear how the use of "characterized" describe or define the condition. Furthermore, the claims are indefinite in the term of "OB resistance" because the mature and make-up of the kind of resistance is not set forth. Does applicants intend for this to be with regard to weight or some other condition that the OB protein has been implicated in?

3b. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 15-18, 20-24, 27-31 and 34-35 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The specification has not provided enablement that would support the claims for a number of reasons. First, with regard to claims 15-17 the teachings in the specification are not sufficient to enable the amelioration of the toxicity of any cytokine by the use of the Ob-R agonist, because the toxicity of the various different cytokines are modulated and regulated differently. These activities can not be regulated one from the other, and there is no evidence, examples or guidance to ensure that the limited studies shown are predicative for all cytokines. Thus, the scope of these claims are not supported by the specification.

Claims 18 and 20-24 read on agents that regulate expression of the Ob-R, however the specification is not enabled for the treatment of obesity with any OB-R expression inducer. This term reads on antisense, ribozymes and other expression regulatory agents, which are not predictive one from the other. But most importantly, the regulation of expression is an unpredictable science. In a similar manner, claims 28-31 are not enabled for the use of any cytokine to increase expression of the Ob-R. The above paragraph about the non-predictability of one cytokine versus another is also equally applicable herein.

In a manner similar to the above rejection under 35 USC 112/2nd paragraph, claim 27 is also not enabled for the scope of the conditions that are characterized by Ob resistance. While it is known that the Ob protein can be used to regulate certain weight disorders and is associated with insulin levels and diabetes, there have been other conditions in which the Ob protein has been implicated. However, each of these condition are not treated or regulated in the same manner. Therefore, in the absence of sufficient evidence, examples or guidance, this specification is not enabled for the scope of the claim limitation.

The specification has not enabled the used of any Ob binding protein, nor the specific use of antibodies to treat anorexia, cachexia or wasting condition. The specification appears to rely on speculation and hypothesis, but fail to provide concrete evidence, examples or guidance to support the claim limitations.

4. Prior art rejections:

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371© of this title before the invention thereof by the applicant for patent.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103© and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

4a. Claims 8-14 and 15-17 are rejected under 35 USC 102(b) as being anticipated by, or in the alternative, under 35 USC 103(a) as being obvious over Friedman et al (`309), Grunfeld et al, Pelleymounter et al or Halaas et al.

The claims are directed to compositions of the Ob protein or an Ob agonist ligand, wherein the claims recited several intended uses for the composition such as regulating energy metabolism during a systemic inflammatory response, or for ameliorating the toxicity of cytokines. Each of the prior art disclose composition of the Ob protein or related protein that are agonist, but the protein is disclosed for use in a different method from those of the claims. The prior art anticipate or render obvious the claims for a composition of the Ob protein irrespective of statements of intended for the composition. Furthermore, a composition per se is not distinct even if it is

used for a different purpose or in a different method. Therefore, the burden is on the applicants to prove that the prior art composition does not possess the properties for methods of treatment consistent with the claims.

4b. Claims 33-35 are rejected under 35 USC 102(b) as being anticipated by, or in the alternative, under 35 USC 103(a) as being obvious over Friedman et a (`309).

In addition to the above teachings, Friedman et al also disclose antibodies to the ob protein and teach that these antibodies can be used in diagnostic methods to detect for disorders associated with the Ob protein. Thus, the prior art appears to meet the claim limitation, irrespective of the fact that the language used to define the invention differs, and irrespective of statements of intended use for the antibody composition.

4c. Claims 28-31 are rejected under 35 USC 102(b) as being anticipated by, or in the alternative, under 35 USC 103(a) as being obvious over Grunfeld et al.

Similar to the above, these claims are directed to a composition of the Ob protein and a cytokine, and wherein the claims recite specific statements of intended use for the composition. Grunfeld et al teach that endotoxin and cytokines induce the expression of leptin/ob in response to infection, and with this discovery, they provide compositions of the Ob protein and cytokines such as TNF, IL-1, Il-6, Il-8 and IFN. The prior art anticipate or render obvious the claims for a composition of the Ob protein and a cytokine irrespective of statements of intended for the composition. Furthermore, the composition per se is not distinct even if it is used for a different purpose or in a different method. Therefore, the burden is on the applicants to prove that the prior art composition does not possess the properties for methods of treatment consistent with the claims.

4d. Claims 1-7, 18-26, 27, 28-31 are rejected under 35 USC 103(a) as being obvious over Grunfeld et al.

The disclosure of Grunfeld et al has been set forth above. Since the prior art teach that endotoxin such as LPS and cytokines induce expression of the Ob protein in response to infection. In view of the well known fact that many infections are associated with or are accompanied by inflammations, at the time of the invention it would have been obvious to use the ob protein alone or in conjunction with the endotoxin or a cytokine to regulate energy metabolism during inflammation that are associated with the ob protein.

5. ***Advisory Information:***

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to **Garnette D. Draper, Art Unit 1646, whose telephone**

number is (703) 308-4232. Examiner Draper can normally be reached Monday through Friday, 9:30 A.M. to 6:00 P.M.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist at telephone number (703) 308-0196.

Official papers filed by fax for this "Pilot for Written Restrictions" should be directed to (703) 305-3704-which is a Fax machine specifically for this pilot. Papers related to this application for election from the written restriction may be submitted to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1 (CM1). The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)). NOTE: If Applicant *does* submit a paper by fax, the original signed copy should be retained by applicant or applicant's representative. **NO DUPLICATE COPIES SHOULD BE SUBMITTED** so as to avoid the processing of duplicate papers in the Office.

GARNETTE D. DRAPER
PRIMARY EXAMINER
GROUP 1800

FILE COPY

Application No.: 09/194889

NOTICE TO COMPLY WITH REQUIREMENTS FOR PATENT APPLICATIONS CONTAINING NUCLEOTIDE SEQUENCE AND/OR AMINO ACID SEQUENCE DISCLOSURES

The nucleotide and/or amino acid sequence disclosure contained in this application does not comply with the requirements for such a disclosure as set forth in 37 C.F.R. 1.821 - 1.825 for the following reason(s)

☐ 1. This application clearly fails to comply with the requirements of 37 C.F.R. 1.821-1.825. Applicant's attention is directed to these regulations, published at 1114 OG 29, May 15, 1990 and at 55 FR 18230, May 1, 1990.

☐ 2. This application does not contain, as a separate part of the disclosure on paper copy, a "Sequence Listing" as required by 37 C.F.R. 1.821(c).

☒ 3. A copy of the "Sequence Listing" in computer readable form has not been submitted as required by 37 C.F.R. 1.821(e).

☐ 4. A copy of the "Sequence Listing" in computer readable form has been submitted. However, the content of the computer readable form does not comply with the requirements of 37 C.F.R. 1.822 and/or 1.823, as indicated on the attached copy of the marked -up "Raw Sequence Listing."

☐ 5. The computer readable form that has been filed with this application has been found to be damaged and/or unreadable as indicated on the attached CRF Diskette Problem Report. A Substitute computer readable form must be submitted as required by 37 C.F.R. 1.825(d).

☐ 6. The paper copy of the "Sequence Listing" is not the same as the computer readable from of the "Sequence Listing" as required by 37 C.F.R. 1.821(e).

☐ 7. Other: _____

Applicant Must Provide:

☒ An Initial or substitute computer readable form (CRF) copy of the "Sequence Listing".

☐ An Initial or substitute paper copy of the "Sequence Listing", as well as an amendment directing its entry into the specification.

☒ A statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d).

For questions regarding compliance to these requirements, please contact:

For Rules Interpretation, call (703) 308-4216
For CRF Submission Help, call (703) 308-4212
For PatentIn software help, call (703) 308-6856

PLEASE RETURN A COPY OF THIS NOTICE WITH YOUR RESPONSE

COPY FOR [ ] File [ ] Applicant